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Strategic evaluations and techno-economic networks. Vaccine innovation in the Cuban biotech sector: for public health – or for profits?

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Abstract

In this paper the Cuban biotech sector with its highly integrated vaccine industry is analyzed in the perspective of the techno-economic network model of Michel Callon. The paper discusses the strategic evaluations that have been performed in the sector. Given the emphasis on public health displayed by the Cuban government and the precarious condition of the Cuban economy (at least during the last 20 years), the strategic evaluations could be seen as an articulation of the (sometimes conflicting) interests of public health and commercialism. The main issue to be discussed in the present paper is how interests related to public health and economic considerations are articulated and balanced in the strategic evaluations that have been made in the Cuban biotech sector. There is a focus on the vaccine related activities of the sector, which will be loosely referred to as the Cuban vaccine industry. This is the first of two papers about the Cuban bitoech sector and vaccine industry.

Keywords: Innovation systems, techno-economic networks, Cuba, vaccines, biotechnology.

Introduction

Cuba is famous for its state-operated, free, universal, comprehensive, and nation-wide public health system, which appears as a strong and highly tangible expression of humanitarianism and philanthropy. Since the early 1980s a biotechnology sector has also been developing, which simultaneously exploits the public health system as a source for inventions and as a testing ground for new drugs, and supplies the public health system with valuable – and sometimes unique – biopharmaceuticals. Vaccines are such an important part of the Cuban biotech sector that one may speak of a vaccine industry embedded and integrated into the biotech sector.

Since the biotech sector is so closely linked to the public health system it could be tempting to assume that the biotech sector is simply at the service of public health, by providing biopharmaceuticals according to needs defined by the public health authorities. However, the Cuban biotech sector not only supplies the domestic health services – it is also a major source of foreign currency revenues of the country. Consequently, the interests or considerations that con-

tributed in shaping the biotech sector may be more diverse than merely that of improving the health status of the Cuban people.

This paper aims to answer a set of questions revolving around how different interests relating to public health and commercialism are articulated and reflected in the Cuban vaccine industry. Which were the stated objectives for creating the biotech sector in the first place? How have interests related to public health, education, science, technology, and economic development been used in legitimizing the Cuban revolutionary government? What considerations prompted initiation of individual vaccine product development projects, and which interests were eventually served by the actual configurations of characteristics of these products? How do such product configurations evolve over time? Have conflicting interests given rise to certain dilemmas or paradoxes, and how have any such predicaments been resolved?

The present paper is the first of two papers about the Cuban vaccine industry, and its main contribution is an analysis based mainly on Michel Callon et al.'s (1992) concepts 'strategic evaluations' and 'techno-economic evaluations'. The vaccine industry is an integral and substantial part of the biotech sector, and by studying it as a case embedded in the case of the biotech sector it becomes possible to make a detailed analysis of the relations between explicitly stated intentions and purposes of the sector at large, the characteristics of the vaccine products, the marketing strategies of the vaccine industry, and its economic impact and significance. Such a broad analysis facilitates identification of and a discussion about the interests that seem to have had the strongest bearing in shaping the Cuban biotech sector with its integrated vaccine industry.

The second paper about the Cuban vaccine industry (Plahte 2010) is also based on Callon's techno-economic networks concept, and focuses on the development, organization, and management of that industry and the biotech sector into which it is integrated.

Vaccine and biotech innovation and interests

The Cuban biotech sector consists of several research and production centers working both in biopharmaceuticals and agricultural biotechnology. In particular the biomedical activities, which include an integrated vaccine industry, have gained international reputation and fame. For instance, the Cuban hepatitis B vaccine is based on state of the art genetic engineering technologies, and the therapeutic cancer vaccines that are under development – of which one is already being marketed – is cutting edge technology of international standards. The sector is a result of a direct government intervention that was initiated in the early 1980s, and could be seen as an amalgamation of long time commitments on part of the Castro regime in education, science and public health.

Coming to grips with abstract phenomena like interests requires a conceptual framework, and this paper approaches the problem from the perspective of innovation systems. There are four different, albeit partly overlapping and complementary, kinds of systems that are studied in the innovation systems studies tradition: national innovation systems, regional innovation systems, sectoral innovation systems, and technological (or techno-economic) systems (Fagerberg 2005). In Malerba's (2005) chapter in *The Oxford Handbook of Innovation* (Fagerberg, et al. 2005) the technological systems literature is counted as a sub-field of the sectoral innovation systems literature, and Carlsson and Stankievicz (1995), Hughes (1989), and Callon (1992) are mentioned as important contributions.

It is the techno-economic network model of Michel Callon (Callon 1991; Callon 1992; Callon, et al. 1992) that will be applied in two papers on this topic. This model is based on

actor-network theory, and some concepts from that body of knowledge will also be used in the following.

Callon's model is particularly applicable whenever – but not exclusively – a government or government agency intervenes with direct operational control in a specific sector or technological field with the aim of promoting development of a range of targeted products (or other tangible results). It thus distinguishes itself from both a traditional R&D funding program on the one hand, in which operational control is absent, and a single-product development program (targeting for instance a nuclear bomb or a fighter aircraft) on the other.

Callon distinguishes between two main types of considerations that are made in the course of such an intervention: the *strategic evaluation*, and the *techno-economic evaluation*. The strategic evaluation is the process of identifying a range of desired products to be developed by the intervention, and the techno-economic evaluation is the process of identifying the actors and other resources that are needed in order to reach those goals, and how to organize them. In other words, the concept of strategic evaluations, understood rather as a continuous, reiterative process than a one-off event, is well suited for the task at hand in the present paper, namely to analyze the strategic choices and their underlying assumptions, interests and considerations.

This paper analyzes and discusses the strategic evaluations that have been performed in the Cuban biotech sector, with a certain focus on the vaccine industry. Obviously, given the emphasis on public health displayed by the Cuban government and the precarious condition of the Cuban economy (at least during the last 20 years), the strategic evaluations could be seen as an articulation of the (sometimes, but not always or necessarily, conflicting) interests of public health and commercialism. The main issue to be discussed in the present paper is how interests related to public health and economic considerations are articulated and balanced in the strategic evaluations that have been made in the Cuban biotech sector. There will be a certain focus on the vaccine related activities of the sector, which will be loosely referred to as the Cuban vaccine industry. As already stated, the other paper is mainly about the techno-economic evaluation, *i.e.* how the Cuban biotech sector and vaccine industry were established, and how they are organized and managed.

Existing literature on Cuban biotech

Although at least three authors and author groups have done in-depth studies of the Cuban biotech sector (Feinsilver 1993; Reid-Henry 2007; Reid-Henry 2008; Thorsteinsdóttir, et al. 2005; Thorsteinsdóttir, et al. 2004b), no analysis in an explicit innovation systems perspective has yet been undertaken.

Feinsilver (1993) is a published doctoral dissertation in political science about the Cuban public health system, and one chapter is devoted to a mainly historical treatise of the Cuban biotech sector, seen in the perspective of the 'symbolic capital' that the Cuban government generates by its investment and dedication to public health and biotechnology. Her approach will be returned to below.

Reid-Henry (2007), frames Cuban biotechnology in more discursive terms, by addressing issues of post-socialism, post-colonialism and transition economies. In other words, the issue is rather how the biotech sector may be interpreted and utilized in such discourses, than which interests that influenced on shaping the sector. Yet, the need for reorientation of foreign eco-

nomic relations upon the collapse of the CMEA[1] in the early 1990s is emphasized, an issue that will also be dealt with in the following.

Thorsteinsdóttir and co-workers ran a major research project on medical biotechnology in developing countries, with Cuba as one case studied, the result of which was published in a special issue of *Nature Biotechnology* (Thorsteinsdóttir, et al. 2004a; Thorsteinsdóttir, et al. 2004b), as well as in a number of other journals (Quach, et al. 2006; Thorsteinsdóttir 2007; Thorsteinsdóttir, et al. 2006; Thorsteinsdóttir, et al. 2007; Thorsteinsdóttir, et al. 2005). These publications give a good comparative picture of national biotech capabilities in the South, and point at long term government support and vision, close linkages to the national public health system, international linkages, and patriotism as key factors for the Cuban success in this field (Thorsteinsdóttir, et al. 2004b). Although a concept from the innovation systems literature – 'user-producer relations' – was applied, the perspective was highly empirical, and was not based on innovation systems or in any other way explicitly related to theoretical approaches.

Reid-Henry's other paper (Reid-Henry 2008) is about the 'epistemic spaces' and 'experimental milieu' prevailing in Cuban biotech, and deals with innovation in the perspective of regional development and scientific cultures, rather than that of innovation systems. Thorsteinsdóttir and co-workers' and Reid-Henry's latter contributions will be dealt with in some more detail in the other Cuba paper.

A guide to the reader

This paper starts with a brief introduction to the concept of the techno-economic network, with an emphasis on strategic evaluations. Then follows a historical description of the situation in Cuba in the fields of education and health, but first and foremost biomedical sciences, when the decision to develop a biotech sector was made around 1980. The assessment of this situation was an important premise for the initial strategic evaluation of the Cuban government. The next section is an analysis of how the interests of public health and commercialization of biotech products have been expressed in public appearances by former President Fidel Castro over the formational 15 year period from 1977 to 1991. Then follows an analysis of the vaccine products portfolio of the Cuban biotech sector. It is assumed that the characteristics of each vaccine product is in part a reflection of the interests that were considered when the decisions to develop each product was made, so that it is possible infer the relative influence of the interests of public health and commercialism on the strategic evaluations. Finally, the economic conditions for import substitution (serving public health interests) and export revenue generation (serving commercialist interests) of vaccine products are discussed.

Strategic evaluations in techno-economic networks

The basic idea of the Cuban biotech sector was to transform the resources of a strong medical science basis into products that could either be useful for the national health system or commercialized in overseas markets, by way of a direct government intervention. In other words, the intervention aimed at transforming the results of a specific knowledge field into a range of socially useful products (and processes). As stated above, two major types of strategic considerations may be identified. The first type – strategic evaluation – involves defining a set of desired products that the intervention should generate. This type of decisions would often precede the intervention itself. Those product targets would then be used as a point of departure for the second type, namely to define the actors, themes and organizational form that would be feasible for generating the targeted products – the techno-economic evaluation. Or in other

[1] CMEA: Council for Mutual Economic Assistance.

words, to identify the scientific, technical and organizational problems that would have to be solved in order to generate the targeted products.

Despite being analytically distinct, in practice these two types of considerations are closely interlinked. Although the strategic evaluation precedes the techno-economic evaluation, the former depends on knowledge about the actors, products, and networks that already exist. Similarly, knowledge emanating from techno-economic evaluations may result in redefinition of the strategic target products, so although an initial strategic evaluation most often precedes the initial techno-economic evaluation, the two continue to evolve in a simultaneous and re-iterative process.

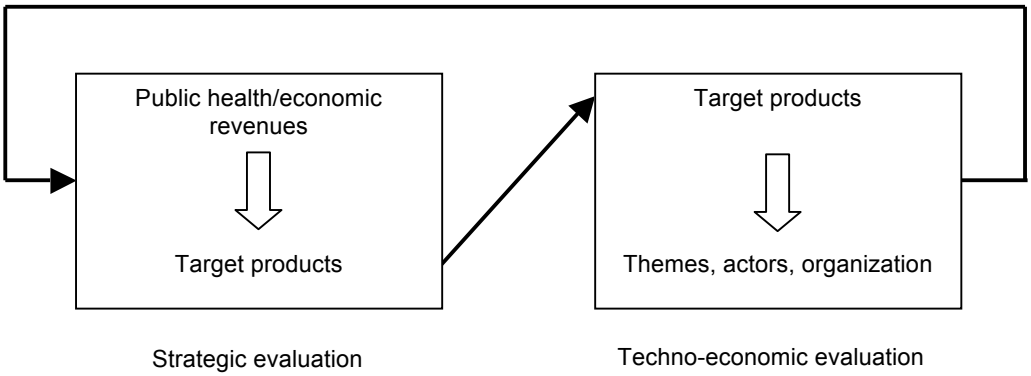

Figure 1. Strategic and techno-economic evaluations. Adapted from Callon et al. (1992).

In the case of the Cuban biotech sector, it was considerations related to public health and economic revenues that motivated the intervention, and in Figure 1 those interests have been inserted into my adaptation of Callon et al.'s (1992) model. In the following sections the issue of strategic evaluations will be approached from three different angles. First we give an account of some aspects of the public health situation in Cuba in the late 1970s that demanded some new solutions.

The socialist revolution and health, education, and science

This section starts with identifying public health as a fundamental political interest of the Cuban revolutionary leadership. Then, a brief description of the national public health situation prior to the initiation of the biotech sector is provided, and the main challenges of the public health system at that time are identified. The dedication to science and education on part of the Castro government is also briefly touched upon, before spelling out the main characteristics of the Cuban biotech sector in some more detail. The section ends with a brief discussion of the main strategic evaluations that have been reflected in the course of this account.

The 'symbolic capital' of health and biotechnology in the revolutionary government

One of the first comprehensive accounts of the Cuban biotech sector was provided by Feinsilver (1993), who devoted an entire chapter of her published Ph.D. dissertation to a historical account of the creation of the biotechnology sector. She relates the creation of the biotech sector, initiated by a pilot project in 1981, to construction of 'symbolic capital' by the Cuban

revolutionary leadership. Although she identifies the concrete and immediate rationale for the biotech initiative …

> The production and exportation of biotechnology, medical and pharmaceutical products was […] employed first and foremost to remedy domestic problems but was capitalized on later to convert acquired knowledge into export earnings. (Feinsilver 1993), p 122

… she argues that the fundamental driving force behind the development of the Cuban health system and the biotechnology sector has been to foster the 'symbolic capital' of the political leadership. In other words, public health has been an intrinsic, high priority national interest. Feinsilver, like myself, several times heard informants speak of former President Fidel Castro as the real minister of health,[2] and she notes that

> […] he has made health indicators the true test of government efficacy and the health of the individual a symbol of the health of the 'body politic'. (Feinsilver 1993), p 200

To a high degree the Cuban government measures its success in terms of basic, but somewhat crude, health indicators: Low infant mortality rates, low general morbidity rates, and high life-expectancy (Feinsilver 1993).[3] Feinsilver also links the biotechnology initiative to Fidel Castro's fundamental belief in science as an instrument for national social and economic development.

The point to be made here is that health and science (and education) has been a top priority for the national leadership in general and for Fidel Castro in particular ever since the insurrection in the late 1950s. We have thus identified one of the fundamental interests of the Cuban political leadership: the public health system has been used by the Castro government as a proof of the success of the revolution.

The point of 'symbolic capital' made by Feinsilver may in fact translate into the terminology of actor-network theory. An important term for conceptualizing power in actor-network theory is 'the Obligatory Passage Point', which is understood as a node in the actor-network that other actors have to pass through in the pursuit of their respective interests (Latour 1987).

The government positions itself at an obligatory passage point between the Cuban population and its access to free and universal health services. The message delivered is in reality that the revolutionary government is the *only* way the actor-networks of the Cuban society may be ordered in such a way that a connection is made between the health services and the *entire* population. Given this priority granted to public health the strategic evaluations performed in relation to the biotech sector would have to align or associate the main objectives or potential benefits of the planned techno-economic networks to this fundamental interest.

The limits of traditional public health interventions

Having now established public health as a fundamental interest in Cuban national policies, the next step is to look at the public health situation by the late 1970s, just before the biotech initiative was embarked upon. How did the concrete public health situation at that time influence on the initial strategic evaluations that preceded the creation of a national biotech sector? And are interests relating to public health entirely unambiguous?

At the take-over in 1959 the Castro government inherited a health system that in reality consisted of four separate health systems; the state hospitals, the private clinics, the mutualist (cooperative) clinics, and the military hospitals, most of which were concentrated to the main

[2] Personal communication with Gustavo Sierra, Vice President, Finlay Institute, 3 February 2009.
[3] Personal communication with José de la Fuente, former Director of Research and Development at CIGB, 11 March 2002.

cities. The health status of the Cuban population in the 1950s, in particular in the rural areas, was characterized by malnourishment, high prevalence of tuberculosis and parasitic diseases, an infant mortality rate of 79 per 1000, and virtually no access to affordable medical services (Feinsilver 1993; Figueras and Pérez 1998).

One of the first major reforms of the Castro government was to create a universal, national public health system. This comprehensive system included primary health care, policlinics, secondary and tertiary care, sanitation, immunization campaigns and programs, and establishment of teaching and research organizations (Feinsilver 1993; Figueras and Pérez 1998).

To cut a long story short, by the 1970s the success of this system resulted in morbidity and mortality patterns in Cuba starting to resemble those of countries in the North rather than the South. The infant mortality rate fell from 38.7 per 1000 in 1970 to 19.6 per 1000 in 1980, and cardiovascular diseases and cancer were replacing infectious diseases as major causes of death (NHSB 1999). Consequently, in order to further reduce the infant mortality rate, congenital disorders would have to be addressed (Feinsilver 1993). In 1975 congenital malformations were not a primary cause of death, but in 1980 they ranked as the third most important cause of perinatal mortality (Majoli 1999).

It was becoming evident that the traditional public health interventions like immunization and sanitation would be insufficient in the efforts for further improvement of the general health indicators. A need for high-tech health interventions like for instance mass screening based on genetic markers and cancer treatment based on modern immunology and genetics was emerging.[4]

In other words, by the late 1970s the existing paradigm of the Cuban public health system was becoming obsolete – a victim of its own success. This public health challenge – a transition from a 'traditional' to a 'modern' mortality and morbidity pattern − should be seen as an important motivation in the initial strategic evaluations preceding the creation of the biotech sector. Existing techno-economic networks were becoming incapable of providing the necessary strategic products for fulfillment of superior political goals of further improvement of the selected health indicators.

Revolutionary science and education

It is not only public health that has been top priorities by the Castro government. In the following another fundamental interest of the Castro government is identified. The much-cited statement by Castro from 1960 …

> The future of our country is by necessity a future of men of science, it has to be a future of men of knowledge, because that is exactly what we are sowing; […]. Sáenz (1990), p 110

… is an early indicator of his belief in the role of science and research in solving social problems.

The other paper gives an account of how a scientific biomedical infrastructure – a Science (S) sub-network in Callon's terms – was developed from the early 1960s. The space here does not allow for more than briefly stating that the educational system was also developed in a comprehensive way, ranging from initiatives like the universal literacy campaign in 1961 to developing a nationwide system for higher education (Brundenius and Monreal 2004). The main point to be made here is that instrumental use of science and education for social and

[4] Personal communication with Roberto Guilarte, Sales Manager at TecnoSuma International S.A., 23 May 2001.

political ends has been a characteristic trait of the political paradigm of the top Cuban leadership.

The Cuban biotech sector

As stated, the other paper gives an account of the creation of a scientific base in biomedicine, and the subsequent creation of the techno-economic networks in biotechnology. Here, let us just take a brief look at the main characteristics of the Cuban biotech sector.

Inspired by a visit to Cuba in 1978 by the US cancer specialist R. Lee Clark President Castro – assisted by the Biological Front that had been established as a consultative body – decided to initiate a pilot project in interferon production. In less than two years the Cubans were producing recombinant interferon for use in clinical trials, and from 1981 several research and production centers were under construction in what must be one of the most ambitious programs for public sector biotechnology development yet to be seen on this planet.

In other words, major techno-economic evaluations were carried out from the late 1970s onwards, and massive investments – a commonly cited figure is USD 1 billion (Reid-Henry 2007) of accumulated investment up to the mid 1990s – secured the creation of the techno-economic networks that may be referred to as the Cuban biotech sector. Today the core of the Cuban biotech sector consists of a handful of research and production centers, all of which connected to the so-called Scientific Pole of Western Havana (hereafter 'the Scientific Pole'). As of 1997 there were 15 scientific poles altogether in Cuba, of which this one is dedicated to biotechnology. More than 60 organizations working in fields that one way or the other are related to biotechnology are connected to the Scientific Pole, among them some specialized hospitals, a consulting company, the national drug regulatory agency (CECMED),[5] a couple of faculties at the University of Havana etc.

The most important of the organizations of the Scientific Pole are located in a western suburb of the capital of Havana. In 1997, when the Scientific Pole consisted of 38 organizations, some 12,000 workers were employed, of which 1,440 were researchers, and 4,046 held university degrees (CITMA 1997). Biotechnology is now the second most important foreign currency income earner, being surpassed by nickel only. The vaccine industry is not a delimited sector, but an integral part of the biotech sector. Several centers fulfill different tasks in vaccine development and production. The most important biotech centers are the Centre for Genetic Engineering and Biotechnology (CIGB),[6] the Finlay Institute,[7] Center for Molecular Immunology (CIM),[8] and Center for Biomolecular Chemistry (CQB).[9]

CIGB is the flagship of the Cuban biotech sector, being as it is by far the biggest organizations, and has its main focus on recombinant technologies based on single cell organisms, and the main products are vaccines as well as other medical, industrial and agricultural biotechnology products.

CIM's focus is on cancer, and its technology platform is recombinant mammalian cell cultures, that is, production of biological substances by inserting genes coding for the desired substances into cell lines taken from mammals.

[5] CECMED: Centro para el Control Estatal de la Calidad de los Medicamentos.
[6] CIGB: Centro de Ingeniería Genética y Biotecnología.
[7] 'Instituto Finlay'
[8] CIM: Centro de Inmunología Molecular.
[9] CQB: Centro de Química Biomolecular.

Finlay's product portfolio is dominated by vaccines based mainly on 'traditional' bacterial fermentation technologies. The institute has several processing lines for bacterial vaccines, and heads the national program for human and veterinary vaccines.

CQB was founded in 2008 by fusing the Center for Pharmaceutical Chemistry with the Center for Synthetic Antigens at the University of Havana into this new entity. The Center for Synthetic Antigens developed a method for industrial production of synthetic haemophilus B (HiB) polysaccharide to be used as the active ingredient (antigen)[10] in the HiB vaccine, which protects against otitis, meningitis and sepsis. The center will work on chemical processes related to biological production, like development of other synthetic antigens and conjugation technologies for vaccines.

Since the 1981 interferon pilot project investments have not only been channeled into founding new biotech centers. In parallel a legal framework has been developed, with patent legislation in operation since 1983, and a drug regulatory agency has been developed and been given increasing independence over the same period (Ratanawijitrasin and Wondemagegnehu 2002).

The initial strategic evaluation

We have seen that the Castro government gave health, education and science primary importance from the very beginning of its reign, and basic health indicators were taken not only as indicative of the health of the population, but also of the success of the government itself. The emphasis on fulfilling the social rights of universal and free access to these services has also been extremely important in legitimizing a regime that has been much less forthcoming in granting its population political rights like freedom of speech and freedom of organization.

However, by the late 1970s the potential of traditional low-tech public health solutions – immunization, sanitation, antibiotics distribution, and primary health care – was depleting. High-tech solutions were called for in order to solve public health problems that were partly on the increase – like cardiovascular diseases – and partly just gaining relative importance as other problem were solved – like congenital disorders.

It is becoming clear that public health considerations are not a singular, unambiguous motivating factor. We have seen that in strategic evaluations that give priority to public health considerations it is sometimes necessary also to decide which types of health problems to address. In their initial strategic evaluations the Cubans were primarily targeting the morbidity pattern of 'modern', 'Northern' societies.

Simultaneously, the CMEA[11] system of the Soviet Union and her political allies constituted a potential export market for reverse-engineered biopharmaceuticals, since intellectual property rights were not being enforced in these countries. So although commercial interests played an important part from the very beginning, it seems like they may have been secondary to public health considerations in the initial strategic decision of establishing the biotech industry.

Let us now approach the question of interests from another angle, by looking at public statements issued by the man that almost personally initiated the Cuban biotech adventure – Fidel Castro himself. It will be demonstrated that economic conditions precipitated a shift – or at least an adjustment – in the balance between public health and commercialism in subsequent strategic evaluations.

[10] The antigen is the substance that is intended to induce a *specific* immune response, i.e. a response directed at the specific microbe that the vaccine is suppose to protect against.
[11] CMEA: Council for Mutual Economic Assistance.

Fidel Castro on the rationale for the biotech sector

This section first presents four different interests that hypothetically could have formed a rationale for developing the biotech sector. Then I examine how those interests are expressed in a selection of former President Fidel Castro's speeches and public appearances over a couple of decades.

Basically, we may speak of three, possibly four, different motivations for creating the biotech sector: one related to public health, another to economic revenues and development, and the third to international collaboration and aid. The (possible) fourth rationale would be Fidel Castro's firm ideological belief in science as a prime force for the transformation of society.

We have already discussed the motivation of public health. The second motivation comes in two versions, although the difference is a somewhat subtle one. Firstly, it is commonly stated that exports were required in order to finance production of biopharmaceuticals for domestic consumption (Lage 2000; Lage 2006). The other is that the aim was to create an economic sector that would contribute to general national economic growth, and that domestic consumption would be a way of legitimizing the generous spending of scarce national economic resources for massive investments in biotechnological research and productive capabilities.

Sáenz (1990) is a compilation of quotes on the topic 'Science, technology and society' from public appearances (speeches and interviews) by Fidel Castro's from 1959 to 1989, and Sáenz (1991) covers the years 1989-91. Based on this publication it was possible to make a simple and somewhat crude analysis of the relative emphasis put on different rationales for creating the biotech sector by the President himself.

The analysis of the quotes in these books referenced by the subject index entries of the term 'biotecnología' shows a clear trend in the direction of more emphasis on economic development as rationale for the biotech initiative from 1990 onwards. There were 35 entries for 'biotecnología', referring to a total of 22 instances of public appearance, and 15 of these included statements about purposes, aims, or rationales for the biotechnology sector.[12] The four purposes relevant for this analysis are 'public health' (national public health considerations), 'economic development', and 'international collaboration or aid', and combinations of these, and 'scientific development'. The frequency of each rationale (and combinations thereof) is listed in Table 1.

Before 1989 economic development was not once mentioned as an independent rationale, while from 1990 onwards biotechnology is given such a role on five different occasions (2nd row). International collaboration or aid stands out with relatively low priority.

There seems to be a shift in rhetoric coinciding with the gradual collapse of the CMEA between 1989 and 1992. This disintegration of international economic relations precipitated a national economic disaster in Cuba, resulting in a 72 percent reduction in imports, a 67 percent reduction in exports, a drop in the investment rate from 26 percent to 7 percent, and a GDP reduction of 33 percent over three years only (Fernández 1999). In the midst of declaring an austerity measures package dubbed 'The Special Period in Time of Peace' President Castro also declared continued dedication to three sectors: food supply, tourism and biotechnology (Sáenz, et al. 1991). Reid-Henry (2007) locates the origin of this reform to the 4th party congress of the Cuban Communist Party in 1991.

Investment in tourism and biotechnology continued throughout the Special Period (which to my knowledge still has not been officially called off); for instance, the Centre for Molecular

[12] In the remaining seven instances biotechnology was related to agriculture or other – for the purpose of this analysis – irrelevant topics.

Immunology (CIM) was inaugurated in 1994, which is commonly regarded as the economic turning point (in other words the year when the Cuban economy touched bottom).

Table 1. Frequency of different stated purposes of the biotechnology initiative in Fidel Castro's public appearances 1977-91.

	Stated rationale of biotechnology initiative	In number of appearances 1977-89	In number of appearances 1990-1
1	Public health	3	1
2	Economic development	0	5
3	International collaboration	0	1
4	Health and economic development	3	1
5	Health and international collaboration	1	0
6	Scientific development (with additional rationale)	1	1
	Total	7	8

Fidel Castro, who had had a close supervision and control of the sector from his State Council office, in about 1993 or 1994 somehow made one step backwards and left the responsibility of the Pole Office to the Secretary of the State Council José Miyar Barrueco.[13] De la Fuente (2001) asserts that this shifts resulted in a more aggressive commercialization by licensing and selling technologies and prioritization of production quality and capacity investments at the cost of research.[14]

The (possible) fourth rationale can be located in the above-cited statement made by Fidel Castro in 1960 about 'men of science' – hence the emphasis of the revolutionary government on science and higher education. It is illustrative of this strategy that the Cuban health system would be based on medical doctors, and not paramedics, or 'barefoot doctors' as in China for instance. Nevertheless, 'scientific development' is mentioned only twice in his 'biotecnología' speeches, and never as an independent rationale.

This analysis demonstrates that throughout the period when the biotech sector was founded (1977-91) Fidel Castro stated both the needs of the public health system and economic development as fundamental rationales for creating the sector. We may, however, observe a certain movement in the direction of more emphasis on commercialization after the CMEA collapse in around 1990, possibly at the cost of public health consideration. In other words, although the initial strategic evaluations were based primarily on public health considerations, in later iterations we may observe a shift towards commercialism, but without in any way losing sight of the former interest.

Interests reflected by the vaccine product portfolio

So far we have looked at the strategic evaluations from the point of view of explicitly stated interests and considerations. It is now time to ask if it is possible to infer the same interests and considerations with the resulting target products as a point of departure. How are different interests reflected by the characteristics of the product portfolio?

The common understanding among my Cuban sources is that the biotech sector works at the service of national needs, and that the public health system is important in defining the priorities of the operations of the sector.

[13] Personal communication with José de la Fuente, 11 March 2002.
[14] Personal communication with anonymous source #1, 3 June 2008.

> These […] centres have the following objectives: 1) to support the health system with high-technology products, and 2) to be economically self-financing in doing this. That is, the main aim is to be socially oriented, and commercialization is the means by which to fulfill that objective.[15]

Some of the early products were very much about solving domestic health problems. The very first biotechnological product development project targeted interferon, a protein that at time was believed to become a 'magic bullet' in the treatment of cancer and viral diseases. The diagnostics equipment MicroSUMA developed at CIE was designed for mass screening of serum samples, targeting both infectious diseases and congenital disorders. Also CIM's initial monoclonal antibody development activities fit into the strategy of targeting a 'Northern' morbidity pattern.

However, an important activity of the Cuban biotech sector is development and production of vaccines, paradoxically enough a product that is associated with 'traditional' infectious diseases rather than with modern, genetically and 'life-style' related illnesses.[16] Another similar, although less fundamental paradox, is that although intended as a measure against 'modern' diseases, the first application of interferon was in the management of the dengue fever epidemic in 1981 – a tropical, and thus 'Southern', infectious disease.[17]

This section examines the vaccine product portfolio of the biotech sector, assuming that interests may be inferred from the product characteristics. However, is it possible to derive or infer interests from pharmaceutical product characteristics? For instance, is it possible to see a strong influence of the national public health system on the biotech sector reflected in that sector's product portfolio? Are there any specific national public health problems being addressed by some unique, specific, and domestically developed biopharmaceuticals? In reality, the issue of interests is not that simple and straightforward. The following paragraphs will reveal that the vaccine product portfolio of the biotech sector reflects a much more complex pattern of motivations, strategies, and historical explanations. Let us look at the vaccines that are currently registered and commercially available from Cuban manufacturers (Table 2).

Meningococcal group B and C vaccine

The other paper about the Cuban biotech sector provides a detailed account of the innovation process resulting in the meningococcal group B and C vaccine, which was developed in order to combat a national epidemic of meningococcal disease, caused by a group B bacterial strain against which there was no vaccine commercially available. The epidemic started in the late 1970s, and the vaccine was applied in a national immunization campaign in 1991. It was developed by the precursor organizations of what is today the Finlay Institute (Valcarcel, et al. 1991).

This is the product that almost in an archetypical way would exemplify a vaccine industry at the service of a national public health system. Nevertheless, subsequently the VA-MENGOC-BC® vaccine turned out to have a commercial potential, and of the 55 million doses have been produced to date, more than 40 million doses have been exported, mainly to other Latin American countries (Sotolongo, et al. 2007). Its commercial potential is limited by the fact that it does not protect against all the group B strains that are circulating globally, so it is not

[15] Personal communication with Agustín Lage, Director of CIM, 11 May 2001.
[16] As a matter of fact, the term 'life-style related illness' could be an equally appropriate label for the traditional infectious diseases, given their intrinsic association with the 'life-style' of poverty and deprivation.
[17] Personal communication with Manuel Limonta, former Director of CIGB, 14 February 2009.

directly applicable as a single group B component in a comprehensive meningococcal vaccine for global use in childhood immunization programs, for instance.

Table 2. Vaccines marketed by Cuban manufacturers.

Trademark	Disease
Finlay Vaccines S.A.:	
vax-TyVi ®	Typhoid fever
VA-MENGOC-BC ®	Meningococcal disease, serogroup B and C
vax-SPIRAL ®	Leptospirosis
DTwP-vaccine	Diphteria, tetanus, pertussis
VA-DIFTET ®	Diphteria, tetanus
vax-TET ®	Tetanus
Heber Biotec S.A.:	
Heberbiovac HB	Hepatitis B
Quimi-HiB	Haemophilus influenzae B
Trivac HB ®	Diphteria, pertussis, hepatitis B
Heberpenta ®	Diphteria, tetanus, pertussis, hepatitis B, haemophilus B
CIMAB S.A.:	
CIMAVax-EGF	Lung cancer (non-small cells)

Hepatitis B vaccine

The recombinant hepatitis B (hepB) vaccine is one of CIGB's early products. A blood based preparation of hepatitis B antigen was successfully tested in animal models in 1983 at a medical research center in Havana, and in 1984 and 1985 different recombinant antigen production techniques were explored. The first batches were produced in 1987 (Pentón, et al. 1994).

In contrast to the group B meningococcal vaccines, which by existing technologies are highly strain specific, hepatitis B vaccines using the surface protein antigen can be applied globally. Hepatitis B was endemic in Cuba as in many other developing countries at that time.

CIGB's Heberbiovac HB is based on modern genetic engineering, but is largely a reverse engineered product very similar to Merck's and SmithKline Beecham's original designs (Milstien and Kaddar 2006). The gene coding for the surface protein is inserted into the genome of bakers' yeast, the yeast is cultivated, and the protein is purified. The Cuban hepatitis B vaccine was registered in 1990, and an immunization campaign directed against children was launched in 1992. The vaccine was also included in the National Childhood Immunization Program (Pentón, et al. 1994). The same year 1.125 mill doses were exported to Colombia (Oramas 2003).

Simultaneously, as a result of extensive vaccine introduction pilot program activities by the Task Force on Hepatitis B Immunization in South East Asia, the World Health Assembly endorsed the inclusion of hepatitis B vaccine in the Expanded Programme on Immunisation (EPI) (Mahoney and Maynard 1999). CIGB's vaccine received its approval for WHO prequalification in 2001.

When hepatitis B immunization started in Cuba in 1992, the incidence rate was 20.3 per 100,000 (Galindo 2004), so an obvious potential public health benefit was present. However, Merck's and SmithKline's vaccines initially cost USD 30 per dose, with a three-dose schedule (Mahoney, et al. 2005), a price that must have been entirely prohibitive at the time of initiat-

ing CIGB's hepatitis B vaccine development project. Thus, there was a rationale for domestic production as an alternative to imports of that vaccine. Simultaneously, the high price must have represented an opportunity for export revenues generation.

Haemophilus B (HiB) vaccine

The Cuban HiB vaccine is a truly novel product, being the world's first vaccine ever to be based on a chemically synthesized antigen. The first conjugate HiB vaccine entered developed country markets in 1987, but the complex production technique as well as sluggish demand in the low-price markets of UNICEF and PAHO contributed to keeping the price up (Chee, et al. 2008). Like with the hepatitis B vaccine, the Cubans decided to develop their own product.

The HiB vaccine became available on the global public sector markets in 1997, and initially it was sold at USD 5 per dose.[18] Already in 1989 two parallel HiB vaccine development projects had been initiated in Cuba, one located at the Finlay Institute based on bacteria culture, and one located at the Laboratory for Synthetic Antigens (LAS)[19] at the University of Havana, based on chemical synthesis.

Synthetic production of the HiB polysaccharide is not a Cuban invention, but the development of the industrial scale manufacturing process was done by the LAS in collaboration with a laboratory at the University of Ottawa in Canada, which co-authored the patent. A conjugation technology was developed by the LAS. The CIGB also participated in the development project (Kaiser 2004).[20]

The HiB vaccine project at the Finlay Institute was abandoned in 2001, when the synthetic product of the LAS entered clinical trials. When imported HiB vaccine was introduced in the Cuban National Childhood Immunization Program in 1998,[21] the incidence rate was about 1.5 per 100,000. The price offered through PAHO's Revolving Fund was at this time USD 2.50 per dose. The Quimi-HiB® vaccine was first distributed domestically in January 2004 (Anon. 2004a). Subsequently exports have been made.[22] WHO-prequalification is pending.

Both the HiB vaccine and the hepatitis B vaccine may be regarded as being part of long-term technology platform development strategies. The HiB vaccine development project, unlike all the other vaccine development projects, was located at a research center at the University of Havana, which underscores the basic research aspects of the project. It also operated with an unusually long time horizon to Cuban standards, and apart from the vaccine itself it resulted in creation of technological capabilities in chemical polysaccharide synthesis. In particular the pneumococcal conjugate vaccine under development at the CQB is based on the chemical technique of polysaccharide conjugation that was developed with the HiB vaccine. Similarly, the hepatitis B vaccine development project at the CIGB pioneered the exploration of several different recombinant protein expression systems, which must have been important experiences on which to found subsequent product development projects based on recombinant technologies.

Like is the case with the hepatitis B vaccine it is easy to identify both import substitution and export earnings generation as important objectives for the HiB vaccine, and it is equally difficult to determine the relative importance of these two rationales.

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[18] Personal communication with Claire Frijs-Madsen, UNICEF Supply Division, 5 June 2009.
[19] LAS: Laboratorio de Antígenos Sintéticos.
[20] Personal communication with Vicente Vérez, Director of CQB, 4 February 2009.
[21] Personal communication with Vicente Vérez, Director of CQB, 4 February 2009.
[22] Personal communication with Vicente Vérez, Director of CQB, 4 February 2009.

The pentavalent DTP-hepB-HiB vaccine

Combination vaccines save on cold chain capacity, on disposables like needled and syringes, and on number of injections required for each child. The pentavalent DTP-hepB-HiB vaccine was offered through the Revolving Fund from 1999 at the price of USD 3.50 per dose (PAHO 2006). Thus, the potential for import substitution was moderate, while the potential for export revenues generation in non-PAHO and non-UNICEF supplied middle-price countries like Russia and China must have been substantial when development of the Cuban pentavalent vaccine was initiated around 1994.

Recently, sales of the pentavalent vaccine have increased dramatically in the low price market served by UNICEF, after a somewhat sluggish introduction period: procured volumes for 2009 are 130 million doses, double that of 2008 (Matthews 2009).

The DTP (the traditional triple vaccine) and the DT combination vaccines are used as booster doses in the Childhood Immunization Program (see Table 3 on page 19). The DTP is also an input for the pentavalent vaccine, and likewise, the antigen of the tetanus monovalent vaccine is used as a carrier protein in Quimi-HiB®. The DT-hepB trivalent combination is not used domestically, and is probably primarily an export commodity.

There is possibly a commercial potential in the DT-hepB trivalent vaccine. The remaining vaccines – the pentavalent, the DT combination, and tetanus monovalent – display a more mixed rationale, like is the case for hepatitis B and HiB.

The typhoid fever vaccine

Finlay Institute's typhoid fever vaccine is a polysaccharide vaccine quite similar to one being marketed by Pasteur Mérieux, and replaced an older Cuban inactivated whole-cell vaccine (Azze, et al. 2003). Typhoid fever vaccine is not in the PAHO Revolving Fund procurement portfolio, so it may be assumed that import prices have been somewhat higher than those of the traditional childhood vaccines, although recently Sur et al. (2009) reports sales of a corresponding vaccine in India at no more than USD 0.50 per dose. The Cuban vax-TyVi® vaccine is presented as a 'low-price' vaccine intended for domestic use, for exports to other developing countries, and as a travelers' or risk groups' vaccine (Azze, et al. 2003).

The leptospirosis vaccine

Leptospirosis is a zoonotic bacterial disease – also known as Weil's disease – which transmits to humans by ingestion of urine of infected rodents, with agricultural workers as one of the high-risk groups. Clinical manifestations range from asymptomatic to relatively rare fatal cases, and it is commonly confused with malaria, dengue fever, yellow fever and others (Bharti, et al. 2003). Incidence rates in Cuba were increasing from 1991 onwards, partly because 'urban' and private backyard farming became widespread as the economic crisis unfolded. Imports of the Soviet vaccine were abandoned, also as a result of the CMEA collaboration collapse.

In my view, Finlay Institute's inactivated whole-cell leptospirosis vaccine should be regarded as a vaccine targeting a domestic health need, although import substitution may also have been an issue. Since the global disease burden and strain epidemiology of leptospirosis is poorly estimated, the potential for exports must have been unclear, at best. It seems like Finlay initiated the development program in 1991, and that the vaccine was registered in 1996 (Martínez, et al. 1998; Martínez, et al. 2000). Since killed whole-cell vaccines are likely to have short-term protection (Bharti, et al. 2003), it is possible that risk groups in Cuba are repeatedly and routinely immunized.

Therapeutic cancer vaccines

By one source CIM's therapeutic cancer vaccines were presented as export oriented products, targeting high-price markets in developed and middle-income countries,[23] while another claimed that the main rationale is to export the products in order to finance domestic use.[24] It remained a bit unclear to me why domestic use of these vaccines should be of such minor importance. One possibility is that the chemotherapy and radiation therapies that have to accompany therapeutic cancer vaccines are simply to costly to be in common use in Cuban hospitals, but this is entirely my own speculation.

Other vaccines

One more product, and two development projects, need mention in order to complete the picture. Finlay Institute is supplying meningococcal group A polysaccharide in bulk for final processing at Biomanguinhos in Brazil, to be distributed by WHO in immunization campaigns in the 'Meningitis Belt' in sub-Saharan Africa. The first shipment of 5.2 million doses was donated (ACN 2008), reflecting a motivation bordering on international aid and medical diplomacy. Another similar project is a recently initiated collaboration with the National Institute of Public Health in Norway for developing a meningococcal group A outer membrane protein vaccine for use in the Meningitis Belt.

The other development project is a genetically attenuated oral cholera vaccine which is currently approaching clinical trials. There is no cholera in Cuba, so this vaccine is intended to combat or prevent cholera epidemics abroad. Gustavo Sierra at Finlay Institute gave me a vivid account of how Fidel Castro one day in 1991 appeared at the recently inaugurated organization with a copy of a news cable reporting the first cases of a cholera outbreak in Peru, declaring that Cuba should develop a cholera vaccine.[25] This project should be seen as an expression of Castro's medical diplomacy ambitions, and its potential benefits for the national public health system are not easy to spot.

Multiple interests – and two paradoxes

An analytical problem is that in most cases it is difficult to distinguish between the interest of domestic needs and that of export earning potentials. The point is that there are very few health problems caused by infectious diseases that are *specific* or *unique* to Cuba. Thus, the vaccine product portfolio reflects the fact that infectious diseases are global health problems, so that most vaccines serving domestic needs also have a commercial potential overseas. The same applies the other way around; in most cases vaccines that have been demanded abroad would also be needed at home. So perhaps one should not expect of a vaccine product portfolio unambiguously to reflect any of these two interests.

It does not come as a surprise then, that this analysis reveals that the product portfolio reflects highly mixed interests. The meningococcal group B and C vaccine and the leptospirosis vaccine are products that were intended for domestic use only, and the subsequent commercial success of the former was neither predicted nor planned for when the vaccine development project was initiated in 1983. The other extreme – almost exclusive focus on overseas markets – is represented by the therapeutic cancer vaccines and the DT-hepB trivalent vaccine. Simi-

[23] Personal communication with Luis Henrique Fernández, Director of Vaccine Department at CIM, 17 September 2008.
[24] Personal communication with Rolando Pérez, Director of R&D at CIM, 5 May 2009.
[25] Personal communication with Gustavo Sierra, Vice-President at Finlay Institute, 3 February 2009.

larly, the hepatitis B vaccine is an expression of a desire to combat a 'traditional' morbidity pattern, while the cancer vaccines target illnesses of the 'modern' pattern.

The production of bulk meningococcal group A polysaccharide stands as a borderline case between commercialism and medical diplomacy, while the cholera vaccine that is under development is an expression of the latter. Development of technology platforms seems to have been additional rationales for both the hepatitis B and HiB vaccines.

The other vaccines seem to have been intended both for domestic use and for exportation. To put it short, in the different strategic evaluations the selection of products has been influenced by a mix of interests. The relative emphasis of considerations of public health and commercialism has differed between the various vaccine products in the product portfolio, with technology development and medical diplomacy as additional motivations for some vaccines.

There is a paradox that although the biotech sector was established with the initial motivation of addressing new, 'Northern' health problems, a vaccine industry emerged as an important part of the sector, developing a product portfolio that almost by definition addresses more 'Southerly' associated, infectious diseases. How come that vaccines have become so important? The other paper will demonstrate that the Cuban biotech sector was not designed based on strategic interests and scientific opportunities alone. The serious and acute public health problem of the meningococcal epidemic called for a biopharmaceutical solution that would turn out to have irreversible consequences in terms of the organization, functioning and product portfolio of the emerging techno-economic network.

Another paradox is that when the vaccine industry eventually started to target the 'Northern' health problems that were the initial rationale for the biotech initiative – with the introduction of therapeutic cancer vaccines – the emerging products seem not to be intended for the domestic market, but are targeting high-price export markets in high-income countries.

Opportunity cost, import substitution and export earnings

Having now studied the considerations underlying the strategic evaluations in Cuban biotech – with a focus on the vaccine industry – by first looking at explicitly stated rationales and then at the interests reflected by the portfolio of vaccine products, in this section we will look at the interests surrounding the strategic evaluations from yet another angle, by analyzing the economic conditions imposed on the Cuban vaccine industry by the international and domestic vaccine markets. The main question to be addressed is whether domestic vaccine manufacturing primarily contributes to substituting imports, or if it is in terms of export revenue generation that it has the most important economic impact. It may be possible to infer underlying interests from such an analysis. In the previous section the issue was to reconstruct the considerations as they may have appeared at the point in time when the strategic evaluations were in fact undertaken, while the task now at hand is to assess the actual economic impact as seen in retrospect.

In this section we will be looking at both strategic and techno-economic evaluations. The reason for dealing with both almost simultaneously is that while the selection of particular products with more or less known characteristics, like for instance commercial potential, is part of strategic evaluations, the choice of a particular marketing strategy, for instance by deciding to develop exports into some markets and not others, is part of the techno-economic evaluation. Again, we observe that although the two types of evaluation are fairly easy to distinguish from each other in principle, in practice they turn out to be more intertwined.

As stated in the introductory paragraphs of this paper the techno-economic evaluations are about how to intervene in and develop the three main sub-networks science (S), technology

(T), and market (M), as well as the intermediary sub-networks S-T and T-M. In these theoretical terms, the techno-economic issue to be discussed here is how the Cuban vaccine industry relates to domestic and overseas markets (M), or in other words, how the T-M sub-network is used and developed in order to connect to or relate to the international part of the sub-network of the vaccine markets (M).

First, the dilemma of opportunity cost is developed. Then, the value of import substitution generated by the Cuban vaccine industry is estimated, and it is demonstrated that it is difficult to economically justify the massive costs of investment by reference to these benefits. The next paragraphs study how the marketing strategy of the Cuban vaccine industry seems to try and resolve the opportunity cost problem, *i.e.* it is asked what techno-economic evaluations that have been made. The final part of this section makes some rough estimates of the value of Cuban vaccine exports. Based on these findings the concluding paragraphs attempt at casting light on the questions of the interests underlying the strategic evaluations that resulted in the selection of these vaccine products.

The problem of opportunity cost

The problem of opportunity cost arises from the fact that Cuba has access to very low-priced vaccines through the Revolving Fund of the Pan American Health Organization (PAHO). This problem confronts vaccine manufacturers in all countries that have access to the low-revenue markets represented by PAHO's and UNICEF's vaccine procurement services. Except for the meningococcal group B vaccine, the leptospirosis vaccine, and possibly the typhoid fever vaccine all vaccines currently in use in routine immunization in Cuba are commercially available in low-price international public sector markets. With vaccines imports available close to marginal costs, why then establish domestic development and manufacturing capabilities? Or in other words, what kinds of economic interests are currently being served by the domestic manufacturing of these products?

We saw in Table 2 on page 13 that in total the Cuban vaccine industry holds a portfolio of 12 registered vaccines for human use. Ten of these are used in the National Childhood Immunization Program. The one against the zoonosis leptospirosis is used in risk groups, like agricultural workers, and the last one is a therapeutic cancer vaccine manufactured by CIM. Heber Biotec also markets a veterinary vaccine, GAVAC, for use against a tick-borne disease in cattle. The first step in the following analysis is to estimate the value of the domestically manufactured vaccine products (for human use) in terms of import substitution.

The Cuban National Childhood Immunization Program

The Cuban National Childhood Immunization Program covers twelve diseases: tuberculosis, diphtheria, tetanus, pertussis, hepatitis B, *Haemophilus influenzae* type B (HiB), meningococcal disease, mumps, measles, rubella, typhoid fever, and polio (Anon. 1997; Anon. 2004b).[26] Eleven different vaccines are used, see Table 3. In the public health system Cuban products are consistently preferred to imported products.

In addition to routine immunization, immunization campaigns are sometimes carried out. For instance, in 2004 the Ministry of Health distributed some 1.4 million doses of MMR vaccines for a campaign directed at adolescents, at a total cost of about USD 2 million (Armas and Gómez 2007). Also foreign student residing in Cuba are routinely immunized with MMR, hepatitis B, and tetanus vaccines. And the high volume of tetanus vaccine application proba-

[26] Cuban documents, like Reed (2007), list 13 diseases by counting the meningococcal group B and C bacterial strains as two separate disease agents.

bly means that it is used as a prophylaxis in the treatment of minor and major wounds in the public health system. The coverage rate for the childhood vaccines range from 94 percent for HiB to 99 percent for most of the others,[27] a figure that ranks among the highest in the world.

Table 3. Vaccines used in the Cuban National Childhood Immunization Program, and estimated value of imports and import substitution for 2007.

Vaccine	No. of doses pr person	Given at age	Origin	No. of doses pr year	Price per dose, (USD)	Import cost (USD)	Imports saved (USD)
BCG (tuberculosis)	1	At birth	Imported	111 854	0.1036	11 588	
hepB	1	At birth	Domestic	182 683	0.2343		42 803
Polio	4	At birth, 11 months, 3 and 9 years	Imported	507 040	0.1478	74 941	
DTP-hepB-HiB*	3	2, 4 and 6 months	Domestic	103 278	3.9200		1 214 549
Mening. B and C	2	3 and 5 months	Domestic	110 590	n.a.		n.a.
MMR (measles, mumps, rubella)	2	12 months and 6 years	Imported	113 751	0.9000	204 752	
HiB	1	18 months	Domestic	108 216	3.1500		340 880
DTP	1	18 months	Domestic	72 392	0.1580		11 438
Diphtheria and tetanus	1	6 years	Domestic	133 470	0.0891		11 892
Tetanus	1	14 years	Domestic	951 204	0.0645		61 353
Typhoid fever	3	10, 13 and 16 years	Domestic	472 788	n.a.		n.a.
Sum						291 280	1 682 915

* The pentavalent vaccine

Sources:
The Cuban National Immunization Program: Reed (2007)
Number of doses per year: ONE (2008a)
Vaccine prices: PAHO (2007)

As already stated, Cuba has access to vaccine purchases through the Revolving Fund of the Pan American Health Organization. Apart from broad operational and technical assistance, the Revolving Fund requests bids from vaccine suppliers based on regional forecast and demand, and procures vaccines on behalf of the member countries. PAHO charges a 3 percent fee, which is used to capitalize the fund. The fund capital is used to forward payment of deliveries, and thus ensures liquidity, and no country may place new orders until their account is in balance (Andrus, et al. 2008). The vaccine suppliers offer their vaccines close to marginal cost, which is sometimes just 1/200 of the price the same vaccine may be sold at in Northern markets (Plahte 2005).

The Revolving Fund is a double edged sword for Cuba. On the one hand (or edge), vaccines that are not domestically produced are available at a low cost. The BCG and MMR vaccines are sold at around USD 0.10 per dose, for instance, and it may be estimated based on PAHO's price list for 2007 that Cuba's total human vaccines imports for that year cost about USD 291,000.

On the other hand, such low vaccine prices reduce the potential value of domestic vaccine manufacturing intended for import substitution. Based on the same price list, we may estimate

[27] However, although the reported rate for the 3rd DTP dose is 99 percent, the figure of 72 392 for the 4th shot at 18 months is in fact closer to 60 percent, but the 4th shot is not reported in WHO's statistics. Apart from that, the reported vaccine spending figures and coverage rates correspond well to a control estimate I calculated on the basis of the size of the birth cohorts.

the value of import substitution of the vaccines that are available through PAHO at no more than USD 1.7 million in 2007. The lion's share of that value stems from the pentavalent DTP-hepB-HiB vaccine.

The value of substituting imports of the typhoid fever vaccine is more difficult to estimate, since it is not procured by PAHO, and public price lists do not exist. However, Sur et al. (2009) states that a typhoid vaccine similar to the Cuban product costs USD 0.50 in India. Both Sanofi Pasteur and GSK, as well as several manufacturers in India, Vietnam and China, market such capsular typhoid vaccines. Since India and Cuba both have per capita GDPs just above the USD 1000 mark, it should be quite safe to assume that overseas vaccine manufacturers would be willing to supply the Cuban public sector market at a similar price. In that case, the Cuban typhoid fever vaccine saves imports worth about USD 236,000. Added up with the value of import substitution of the other vaccines, the Cuban vaccine industry substitutes imports of about USD 2 million in total.

Lastly, the unique group B component of the meningococcal B and C vaccine is impossible to value in terms of import substitution, so the value of this vaccine may only be estimated in terms of its public health impact, which of course is beyond the scope of this analysis.

It should be noted, however, that when some of these vaccines came on the market, the price was extremely high. The initial price of the recombinant hepatitis B vaccine was USD 30 per dose when it exited Merck's pipeline in the early 1980s (Mahoney, et al. 2005), and in 1993, when it was offered through UNICEF for the first time, it still cost USD 2.07.[28] The Cuban hepatitis B vaccine was licensed in 1992.

Note also that the above figures do not reflect the full imports expenditures related to immunization activities in Cuba. In addition to vaccines, there will be purchases of syringes, refrigerators and other cold chain equipment, as well as operational costs related to planning, procurement, storage, distribution, epidemiological surveillance, adverse effects monitoring etc. Most of the cold chain equipment used in Cuba is imported. The annual total cost of the immunization program was estimated to about USD 18 million for 2006, of which about USD 12 million were spent on vaccines and supplies (MINSAP 2006).[29]

The point to be made is to formulate the problem of opportunity cost: since vaccines may be imported at a price close to marginal cost, how can it be made economically justifiable to establish development and manufacturing capabilities for such products? Or put slightly differently: since it may hardly be defended to invest hundreds of millions US dollars in vaccine development and manufacturing capabilities in order to save 2–3 millions annually, in what other ways is the vaccine industry justified? Which strategic and techno-economic evaluations may be undertaken in solving this problem?

Firstly, at the time of initiating the development of several of these vaccines the world market prices were very high, and establishing domestic production capabilities could be regarded as a relatively attractive option. However, both the HiB vaccine and the hepatitis B vaccine have been subject to substantial price reductions since their initial introduction – in the case of hepatitis B the price has dropped from the initial USD 30 per dose price through the above USD 2.07 per dose price in 1993, to today's PAHO offer of USD 0.27 per dose (PAHO 2009). Thus, the problem arises in the medium to long term; international competition sharpens as additional suppliers enter the market with identical products, in line with traditional product cycle theory.

[28] Personal communication with Alison Rowe, GAVI, 20 January 2009.
[29] It is not stated how the domestically manufactured vaccines were valued in this estimate.

In other words, the initial strategic evaluation – resulting in a decision to develop a product whose price in the international marketplace is prohibitively high at the outset – is being undermined by decreasing international prices, which in turn calls for techno-economic evaluations in order to solve the emerging problem of reduced savings from the import substituting domestic manufacturing.

Second, the following paragraphs will reveal that the solution to the opportunity cost problem is commercialism and exportation. But which markets may be targeted when UNICEF and PAHO are flooding the markets of most of the countries in the South with vaccine products at rock-bottom prices, and the Northern markets purchase their vaccines almost exclusively from Northern suppliers?

While strategic evaluations are about selecting the products to be targeted by an intervention, techno-economic evaluations are about how to order and engineer the techno-economic networks in order to reach those targets. The choice of market outlets implies establishing relations between T and M, or to construct the M sub-network itself.

The marketing strategy of the Cuban vaccine industry

Which techno-economic evaluations have been made concerning the marketing strategy of the Cuban vaccine industry? Are there any markets open to Cuban exports in which the price margins allow for full or partial recuperation of costs and investments?

Firstly, the Cuban vaccine industry is not targeting the global public sector markets,[30] *i.e.* the low-revenue markets that are dominated by the procurement services of PAHO's Revolving Fund, which was mentioned above, and UNICEF's Supply Division, which purchases vaccines on behalf of African and Asian countries (Andrus, et al. 2008). According to the annual reports of UNICEF Supply Division[31] the only vaccine supplies originating in Cuba were Heber Biotech's (CIGB's commercial arm) sales of not more than about USD 1 million worth in total, most probably hepatitis B vaccine, in 2004-6. Based on UNICEF's hepatitis B vaccine prices for these years this corresponds to some 4.2 million doses only. CIGB's hepatitis B vaccine received its WHO-prequalification approval in 2001 (Oramas 2003). It is not known if CIGB has sold hepatitis B vaccine to PAHO.

Let us look at the hepatitis B vaccine again. As a result of something that appears to be a work accident by the censorship authorities, a table appeared in the regional statistics section of the 2008 CD-ROM edition of the Cuban Annual Statistical Yearbook in which production figures for some selected industrial products originating in the Playa municipality in western Havana were quoted, among them CIGB's hepatitis B vaccine. Average annual output is 13 million doses for the years 2002-7 (ONE 2008b), which is comparable, albeit not directly corresponding, to the Lopez et al. (2006) figures of average annual exports of ten million doses. According to Table 3 above annual domestic consumption is about 290,000 doses (ONE 2008a). So where do these exports go? Which markets are tapped into in order to achieve the average price of USD 2.20 per dose quoted by Lopez et al. (2006) – almost ten times the going rate on the global public sector markets?

Biopharmaceutical exports are not listed in Cuba's export statistics. The only information CIGB representatives have been willing to provide on the topic of their main markets, is that they primarily target middle-income countries that are 'not eligible for the EPI, like Venezu-

[30] Personal communication with Eduardo Martínez, Director of Development Unit, and Yair Quiñones, both CIGB, 19 September 2008.
[31] Contracts worth less than USD 100,000 are not included in these reports.

ela and Argentina et cetera'.[32] However, both Venezuela and Argentina, like all other Latin American countries except for Mexico, have access to vaccines through PAHO's Revolving Fund (Andrus, et al. 2008) at a price close to one tenth of CIGB's average price. It is possible that vaccines have been sold to Venezuela and Argentina independently of the Revolving Fund's procurement services, but at a price very close to the PAHO price. After all, the USD 2.20 per dose price is an average price, and still higher prices may have been charged of other buyers. Yet another possibility is that the sales to Venezuela and Argentina are parts of comprehensive bilateral cooperation agreements that also cover trade and exchange of other products and services. And finally, vaccines may have been sold to the private retail markets of these countries at higher prices than those charged through PAHO.

In an analysis of international vaccine trade patterns Da Silva (2009) identifies the following countries as importers of Cuban vaccines in 1996: Argentina, Brazil, El Salvador, Columbia, Chile, and Mexico. The volumes and prices are not listed.

Apart from Venezuela and Argentina, the Cuban vaccine industry does have some other potential markets. According to one source Russia, China, South Korea and South Africa are main customers of Cuban vaccines.[33] This source could not say anything about the prices charged in these markets.

Let us look at how this information fits with some basic intelligence about the global vaccine markets. Say we make a list of potential markets for Cuban vaccines: countries that are open to vaccine imports from non-Northern suppliers – which in practice excludes the entire OECD-area – and that have either middle to high BNP per capita, or large populations, *and* are not using UNICEF's or PAHO's procurement services. That list includes Mexico, China, South Korea, Thailand, Singapore, Iran, Saudi-Arabia, the United Arab Emirates, Egypt, Libya, South Africa, Russia, and Belarus.[34] Of these, Saudi Arabia, the United Arab Emirates and five other Arab countries have formed the Gulf Cooperation Model, which is a joint vaccine procurement operation similar to that of UNICEF and PAHO (Andrus, et al. 2008). The prices offered in this market are not known to this author, neither are the suppliers. We are left with Belarus, Mexico, Thailand, Singapore, Iran, Russia, China, South Korea, and South Africa. The last four of these were mentioned by my anonymous source above.

Middle and low income countries represent in general two market segments: the public sector market, and the private retail market. Although prices in the former can be very low, in particular in those countries that use UNICEF or PAHO procurement services, private retail vaccine markets in low and middle income countries can be on level with corresponding markets in high income countries, that is USD 10 per dose and upwards. As already stated, one may speculate that Cuban vaccine manufacturers make some of their revenues in private retail markets in Latin American countries, as well as in the four countries that were mentioned above.

The multinational vaccine manufacturers operating out of countries in the North use the mechanism of tiered prices by facilitating low-price high-volume sales to UNICEF and PAHO by charging high prices in their low-volume home markets (most probably, the multinationals export into middle-price markets also). In other words, since they are mainly private companies with access to public and private high-price home markets, they do not face the same opportunity cost problem as their Cuban counterparts. In contrast, as vaccine products

[32] Personal communication with Eduardo Martínez, Director of Development Unit, and Yair Quiñones, both CIGB, 19 September 2008.
[33] Personal communication with anonymous source #1, 29 April 2009.
[34] Based on a map graphic appearing in Matthews (2008).

'mature' on the global markets the Cuban vaccine industry is facing increasing price competition, calling for techno-economic evaluations about how to extend their T-M activities into new overseas markets where higher profit margins may be defended.

We will now make some rough estimates of the export earnings of the Cuban vaccine industry. What is the economic impact of the marketing strategy of the Cuban vaccine industry – resulting from a techno-economic evaluation – of directing the marketing activities into a few selected middle-income country markets (M)?

Export earnings

If it is cumbersome to calculate the imports expenditure, then estimating the export earnings of the Cuban biotech sector is a real challenge. Figures on prices, quantities and revenues are regarded state secrets, and are not quoted in the statistics of the National Statistics Office (ONE)[35] or any other official publications. The biotech centers do not publish annual reports or anything of that sort.

Nevertheless, as stated above, in a rare instance of openness, a group of senior executives and scientists at the CIGB disclosed that

> $220m worth of [HepB] vaccine were sold in ten years and 100 million doses have been used. (Lopez, et al. 2006), p 8 [36]

It is not clear which ten-year period that is being referred to, but supported by information from an anonymous source I assume that it is the ten years prior to the publication: 1996 – 2005. The annual average would be ten million doses, and average annual revenues would be USD 22 million.

The Finlay Institute's meningococcal group B and C vaccine is the world's only group B meningococcal vaccine commercially available.[37] It has been sold in 15 different countries, in a total of 55 million doses (Sotolongo, et al. 2007), 40 million of which before 1997 (Anon. 1998). The only source that supplies any financial information about these sales, is Feinsilver (1993), and her conflicting sources quote per dose prices for the initial sales to Brazil in 1989-91 within the USD 5.50 – 10.00 bracket. Assuming that the initial sales to Brazil are representative of the prices that were obtained in all subsequent contracts, average annual revenues from VA-MENGOC-BC® sales may thus be estimated to be in the USD 22.2 – 40.4 million bracket for the 1989-97 period, and in the USD 6.9 – 12.5 million bracket for the 1998-2007 period. Accumulated revenues of VA-MENGOC-BC® exports from 1989 to 2007 would end up in the USD 271 – 494 million bracket.[38]

Much less is known about the Cuban HiB vaccine and the pentavalent vaccine. The Quimi-HiB® vaccine was first distributed domestically in January 2004 (Anon. 2004a). Subsequently exports have been made,[39] and WHO-prequalification is pending. The pentavalent DTP-HepB-HiB combination vaccine was licensed in Cuba in 2004, and WHO-prequalification is pending on this vaccine also. Export figures for these vaccines, or for any other of the Cuban vaccines, are not available.

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[35] ONE: Oficina Nacional de Estadísticas.

[36] This is the only financial figure that was provided in the entire paper, despite its appearance in the Journal of *Commercial* Biotechnology …

[37] A similar vaccine was developed by Chiron Vaccines in collaboration with the Norwegian National Institute of Public Health for use in New Zealand, but to my knowledge that vaccine has not been registered outside New Zealand. See case study on page **Error! Bookmark not defined.**.

[38] Estimated domestic consumption subtracted.

[39] Personal communication with Vicente Vérez, Director of CQB, 4 February 2009.

Economic impact of the vaccine industry

Based on these somewhat fragmented figures it is at least possible to make a rough estimate the total average annual export earnings of the hepatitis B and the meningococcal group B and C vaccines for the 1998–2005 period. During that period the average annual revenues were USD 22 million for the hepB vaccine, and USD 6.9–12.5 for the meningococcal group B and C vaccine, totaling approximately USD 28.9 – 34.5 per year. Exports of other vaccines could be added, but as stated, no figures are available.

This analysis suggests that the value of vaccine import substitution is one order of magnitude less than the value of vaccine exports. So in terms of economic impact the exports vastly outweigh import substitution. It should also be assumed that Heber Biotec will be able to introduce the new hepatitis B antigen containing pentavalent DTP-hepB-HiB vaccine on the same markets that are now exploited by the monovalent hepatitis B vaccine, so the same effect may be anticipated for that product.

It was tentatively concluded above that the product characteristics reflected a multitude of interests. The analysis of former President Castro's speeches identified a certain shift in the balance between stated rationales of the massive investments into the biotech industry in the direction of stronger emphasis on commercialism after the onset of the national recession from 1990 onwards. The analysis of the actual economic impact of the most important vaccine product demonstrates that the commercial impact of exporting it is disproportionately higher than its impact in terms of substituting imports for the National Childhood Immunization Program. Or in other words, most of the public health impact of that program could theoretically have been achieved at a cost that is much lower than the value of the vaccine exports.

In this light, does it make sense to speak of the vaccine industry as science and technology at the service of domestic public health needs – as my Cuban sources quite consistently do? In terms of actual economic effects, is it not rather the case that the vaccine industry is highly export oriented, and that a production surplus – subsidized by these exports – is transferred to and consumed by the national public health system?

And following this line of thought, would it not be fair to argue that development and production of vaccines that are used domestically serve as political legitimization for the huge investments that have been made in the biotech sector. By the nationally universal distribution of domestically manufactured vaccines the entire Cuban population gets access to tangible results of the biotech sector in a way it would not if other products were exported in order to purchase imported vaccines. And Cuban authorities emphasize that the public health system is always a prioritized recipient, and that only the 'surplus' left after the domestic needs have been met that is exported.

In this respect vaccines have the virtue of being administered to the whole population, as opposed to most therapeutic drugs, which enhances the 'visibility' of that intervention in the population. Moreover, the fact that the vaccines are used domestically is a strong motivational factor for the scientists and workers in the biotech sector, but in my view this is rather a consequence of, rather than a rationale for, domestic use of the products.

Another matter that puts domestic consumption in an instrumentalist light, is international drug regulatory requirements that make the pathway to vaccine exportation conditional upon prior domestic registration and use of the vaccine (Srinivas 2006).[40] This underscores the

[40] See also the decision centered vaccine innovation model paper on page **Error! Bookmark not defined.**.

importance of preferring domestically manufactured vaccines to imported products by the National Childhood Vaccine Program.

Other biotech exports

We now turn to the economics of a few non-vaccine products manufactured by the Cuban biotech sector. Data on the total exports earnings of the biotech sector is no easier to access than data on vaccine exports. Nevertheless, one source stated that the value of total exports for 2008 was USD 50 million for the CIM, and somewhat less for the Finlay Institute and CIGB respectively, in total some USD 150 million.[41] Another source stated that CIGB's annual total export earnings oscillated between USD 28 and 40 million over the last five years, with a growing trend.[42]

It seems like the product portfolios of CIM and the CIGB include some low-investment 'bread-and-butter' product intended as stable cash earners. For CIM this would be recombinant erythropoietin (a growth factor stimulating the production of red blood cells) and a growth factor stimulating white blood cell production.[43] CIGB's corresponding product would be recombinant streptokinase, which is used for dissolving thromboses. Other exported products are interferons marketed by the CIGB, and monoclonal antibodies sold by CIM. The last product to be mentioned here is the diagnostics equipment SUMA, developed and marketed by the Center for Immunoassays (CIE),[44] whose expected export revenues for 2001 were about USD 2.5 – 3 million.[45]

Cuban biotech also gains some revenue from technology licensing agreements. For instance, CIGB has licensed its yeast based recombinant hepatitis B expression system to both Indian Panacea Biotec (Milstien, et al. 2007) and to an Iranian biotech company – the latter deal also encompassed an *Escherichia coli* expression system and the purification protocols for recombinant streptokinase production (De la Fuente 2001).

Similarly, CIM has established joint venture companies in Canada, China, India and Spain. The activities of these companies include development, production and commercialization of virtually all the product categories in CIM's portfolio: therapeutic cancer vaccines, monoclonal antibodies, and erythropoietin (CIM 2008). Figures on the economic benefits of these activities are not available.

It should be mentioned that for pharmaceuticals other than vaccines price discrimination is highly uncommon (Trouiller, et al. 2002), and prices on international markets are probably much closer to those on Northern markets. In other words, from the perspective of the Cuban government domestic manufacturing of non-vaccine pharmaceuticals is relatively more attractive compared to imports, than what is the case for vaccines.

The exports of the Cuban chemical pharmaceutical industry are quoted in the national statistics, and by applying the official exchange rate for Cuban (non-convertible) peso to the US dollar, the total value for 2007 would amount to about USD 12 million (ONE 2008a).

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[41] Personal communication with Juan Triana, Professor at Centro de Estudios de la Economía Cubana, 27 January 2009.
[42] Personal communication with anonymous source, 29 April 2009.
[43] Personal communication with Rolando Pérez, Director of R&D at CIM, 5 May 2009.
[44] CIE: Centro de Inmunoensayo.
[45] Personal communication with Roberto Guilarte, Sales Manager at TecnoSuma International S.A., 23 May 2001.

Summary, import substitution versus export earnings

In this section the dilemma of opportunity costs in the vaccine industry was identified: import substitution does not save large amounts of foreign currency, because the world market prices are close to marginal costs. Vaccines that are sold at prohibitively high prices initially may experience price reductions of one or two orders of magnitude as the number of international suppliers increase, as the case of the hepatitis B vaccine demonstrates.

This creates challenges for the export strategy: it has been necessary to tap into markets where prices are higher than in the global public sector low-price markets. It seems like the Cubans have managed to exploit vaccine markets in a few middle-income countries with relatively large populations. Consequently, it turns out that the value of exports is one order of magnitude greater than the value of import substitution.

The discussion of this section confirms that in practice it may be difficult to separate strategic evaluations about selection of products on the one hand, from the techno-economic evaluation of developing a marketing strategy on the other.

Two remaining, unresolved issues

In this paper the issue of the interests that underlie the strategic evaluations performed in relation to the Cuban biotech sector has been triangulated: first the issue was illuminated by existing literature, then it was studied by analyzing the content of Fidel Castro's public appearances during the decisive period when the sector was created, then the interests were inferred from the characteristics of the Cuban vaccine products portfolio, and finally the issue was approached in an economic perspective.

Before making some concluding remarks two issues that have been identified need some further elaboration. First, despite the emphasis on the emerging modern morbidity pattern in the initial strategic evaluations, the biotech sector developed a vaccine industry that to a high degree has been targeting diseases that are rather a part of a traditional morbidity pattern. This will be elaborated upon in the other paper.

Second, the Cuban vaccine industry has not supplied any substantial quantities of vaccines through the procurement services of UNICEF and PAHO. This is paradoxical in several ways, as the following paragraphs will demonstrate.

The great paradox

We have identified a strong emphasis on national public health considerations, particularly in relation to the initial strategic evaluations. Referencing Feinsilver (1993; 2006), a substantial emphasis on international medical diplomacy has also been identified. In (Plahte 2005) it was demonstrated that vaccine sales into high-volume low-price markets could be profitable. Then why has not CIGB's hepatitis B vaccine been marketed by way of UNICEF's and PAHO's procurement services?

Such a tactic would not only have contributed to improving the public health in the poorest countries of the world, it would also have reinforced the image of Cuba as a 'world medical power', as Feinsilver puts it. Moreover, in theory selling at tiered prices can be of great benefit to the manufacturer, even when the low-price market price approaches marginal cost. And given Cuba's extremely precarious foreign currency balance situation, one should expect that every possibility for making an 'extra buck' would be exploited. One of my sources states that

Cuba would readily sell to any interested buyer.[46] Would it not be a strange twist of irony that vaccine manufacturers of socialist Cuba join ranks with those of capitalist (and political) arch-enemy the USA in refraining from supplying these markets? Lastly, and similarly, to some readers it may appear a bit paradoxical that a self-declared socialist actor distributes its life-saving medical products according to purchasing power rather than need, in particular since the global public sector markets – in theory – could have been profitably served, and as a complement – not an alternative – to serving the middle-price markets.

Plahte (Plahte 2005) lists three preconditions that have to be fulfilled in order to make the tiered pricing mechanism a win-win-*win* situation: the demand structures have to be different in the two markets, there must be no re-sales from one market to the other, and there must be diminishing marginal costs to scale. We should also be aware that the global public sector markets are highly competitive, despite UNICEF's recent shift of policy of purchasing vaccines according to a price bracket including up to four suppliers for each vaccine, instead of its previous practice of going unilaterally for the lowest bid for each vaccine product (Matthews 2008). UNICEF and PAHO obtain prices on a comparable – if not exactly the same – level. So marginal costs must not only be diminishing to scale, costs must be sufficiently low also in absolute terms.

The two first preconditions apply equally to Cuban vaccines as they do to vaccines from any other supplier. In other words, the answer may be found in the cost structure of the Cuban vaccine. There is the possibility that the CIGB is simply unable to manufacture its hepatitis B vaccine at a sufficiently low cost – in absolute terms – to sell profitably to UNICEF and PAHO. Alternatively but similarly, it is possible that the productive capacity of the Cuban vaccine industry reflects a product function that reaches its marginal cost minimum at a quantity below the level required in order to serve the high-volume low-price markets in addition to the middle-price markets – in which case costs would increase with increasing scale.

Like all other pharmaceutical companies the Cuban biotech centers are extremely secretive about issues relating to production costs, so there is no data to directly support this hypothesis. Neither does UNICEF or PAHO reveal the identity of their bidders or suppliers. It is only by eliminating the alternative hypotheses that we may end up with this one as a residual explanation.

It would be quite untenable to underestimate the Cubans by speculating that they are not aware that tiered pricing may be profitable to the supplier. Price discrimination is a topic covered by most general economics textbooks, so that option should be ruled out.

One could also hypothesize that the Cuban hepatitis B could be of inferior quality, and as such be non-eligible for these markets. However, this option must be ruled out, since the Heberbiovac was prequalified for WHO in 2001.

Another hypothesis is that there could be political reasons for Cuba's absence on the global public sector markets. For instance, one could imagine that Cuban vaccines were marketed as but one element in more comprehensive bilateral trade and cooperation agreements, and that there were no 'surplus' vaccines to be sold on these global markets. The possibility of vaccine shipments as an instrument for supporting international diplomatic relations should not be ruled out. The point is, however, that according to the economic theory underlying the price discrimination mechanism such arrangements would be complementary, and not alternatives, to selling on the low-price high-volume markets, since the diminishing marginal costs to scale in vaccine manufacturing would make it profitable to expand the productive capacity in order to serve these markets – provided that the overall cost level is sufficiently low.

[46] Personal communication with anonymous source #1, 7 May 2009.

Despite the lack of data on costs, there is some circumstantial evidence to support the cost hypothesis. First, on the one hand, the most important factor driving operational costs down is the low cost of highly skilled labor in Cuba. In 2001 the monthly salary of a scientist was only about USD 20, and in 2009 it has been raised to about USD 40. With collective and individual bonuses it may double.[47] These costs can be a bit misleading, however. Many workers in the biotech centers have access to subsidized housing, but it is not clear if these schemes are funded directly by the biotech centers or indirectly by the government. Among the indirect subsidies of labor cost by the state are subsidized public transportation, free education on all levels, free health care, and subsidized food on ration cards.[48]

Second, and on the other hand, since a high proportion of the inputs and technical equipment has to be imported the cost of establishing a bioproduction facility cannot be expected to be much lower in Cuba than in a high income country. It is mainly the cost of property and the cost of constructing the buildings as such that may make a difference. This not only applies to Cuba, but to bioproduction companies in most low and middle income countries.

Third, the extremely strict and unlawful economic embargo imposed by the US Government complicates the provision of inputs to the Cuban biotech sector and vaccine industry, driving costs in a way not experienced by any of its competitor vaccine suppliers on the global vaccine markets. Not only are US suppliers of technical equipment, reagents, culture media, and so on ruled out in the first place, probably resulting both in less supplier competition on the Cuban market than elsewhere, and forced selection of economically sub-optimal technical solutions. Even worse, European or Asian suppliers operating in Cuba risk having the US embargo legislation applied on them to the effect that their US market becomes closed off in retaliation for selling to the Cubans, so the Cubans are very careful about maintaining foreign supplier confidentiality. Moreover, if an overseas non-US supplier is acquired by a US company, the substitution of that supplier's component with another may imply that the entire validation of a production process has to be repeated in order to comply with drug regulatory requirements. All these circumstances contribute to raising both investment and operational costs.

This means that although the productive capacity of the Cuban vaccine industry should reflect a product function whose marginal cost minimum is above the level at which the low-price tier vaccine markets may be profitably supplied, it is possible that even further investment in capacity expansion would not overcome the problems resulting from this hypothetical excessive overall cost level. Or in other words, capacity expansion is useless if the costs in absolute terms nevertheless remain too high for making competitive bids in the low-price markets.

Another related explanation could be that it is the production methods used in manufacturing the hepatitis B vaccine in themselves that are inefficient. A fact that undermines that hypothesis is that Panacea Biotech in India is licensing recombinant protein expression system technology from CIGB for production of the hepatitis B component of its pentavalent DTP-hepB-HiB vaccine (Milstien, et al. 2007).

One last complementary explanation is that the global tendency of switching from multi-dose to single dose vials has created bottlenecks also in the filling facility at BioCEN, which is the center that does the final processing of the hepatitis B vaccine, as also happened in vaccine

[47] Personal communication with Gustavo Sierra, Vice President, Finlay Institute, 3 February 2009.

[48] That being said, for the sake of a balanced account it must be added that public transportation services are both overcrowded and underdeveloped, hard currency is required in order to purchase both university text books and many drugs, and for most Cubans the staple goods that can be acquired by the 'libreta' rationing card must be supplemented by expenditures in both national currency and the convertible 'hard' peso in order to secure an adequate food supply.

manufacturers globally. It is possible that the extra investment that would be required to expand this capacity has not been regarded profitable, since the prices on the global sector markets are close to marginal costs.

In short, for the sheer lack of alternative plausible explanations it is somewhat speculatively concluded that despite the low salaries paid in Cuban biotech, the production costs may be too high to make competitive bids towards UNICEF and PAHO, whose prices can be very close to marginal costs. If this should be the case then, the lack of Cuban supplies to the global public sector markets may be a result of exogenously imposed or also purely technical factors, and not of any purposeful strategic or techno-economic evaluations on part of the Cuban vaccine industry. Note that in theory these cost factors would not preclude competitive bids in the middle-income markets into which the Cuban hepatitis B vaccine is exported if the Cubans are willing to accept lower profit margins than their competitors.

Conclusion

In a historical perspective the Cuban biotechnology sector may be seen as an amalgamation of the government's strategic priorities of education, health, and science. These three areas have received special attention from the revolutionary government since the takeover in 1959. Nevertheless, despite the indisputable and strong personal dedication to these political values on part of the Cuban revolutionary leaders, health in particular has also been used instrumentally in stabilizing and legitimizing the Castro regime. The general message has been that the revolutionary government is *the* guarantee for a universal and free public health system.

Consequently, it was necessary to align the social objectives of the emerging techno-economic networks of the biotech sector to the issue of public health for all. And initially, a main objective of the massive investments in a biotechnological industrial complex was to confront an emerging morbidity and mortality pattern that resulted from a depletion of the existing public health paradigm, which targeted a 'traditional' pattern dominated by infectious diseases. In other words, public health is not an unambiguous interest.

Instrumental use of science and technology for social purposes was a core element in the political thinking of the Cuban government since the early 1960s. Nevertheless, technological and scientific development was not stated as an important objective in its own right in Fidel Castro's public appearances during the years when the biotech sector was created. Instead a shift could be observed by which the relative emphasis on public health diminished somewhat as the need for economic recovery gained importance from about 1990 onwards.

Then a number of paradoxes emerge. Despite the intention of confronting the emerging 'modern' disease pattern of cancer and cardio-vascular and congenital disorders, a main part of the biotech complex – the vaccine industry – made infectious diseases of the 'traditional' morbidity and mortality pattern its main target. Moreover, a vaccine product intended to be used in the combat against a purely national meningococcal group B epidemic, turned out to also yield several hundred US dollars worth of export revenues. The other paper will explore how these two issues in fact may be causally connected to each other.

Also the economic interests surrounding the biotech sector may be ambiguous. A problem that had to be dealt with was that while domestic development and manufacturing of vaccine products that were initially prohibitively expensive on international markets could be defended on economic grounds, subsequent price reductions also reduced the value of these products as import substitution factors. Simultaneous pressures resulting from the national economic recession following the collapse of the East Bloc created a need for generating eco-

nomic surpluses, and since high price markets in the North were not accessible high price markets in middle income countries were exploited.

The interests underlying the strategic evaluations that selected the vaccine targets are not necessarily those that eventually are served by the actual socio-economic impact of the resulting products. The export strategies have been so successful that the export revenues outnumber the value of import substitution by one order of magnitude.

The domestic public health system is the priority recipient of the biotech sector products, at a very low cost. Thus, it is necessary to tap into middle-price or high-price markets in order to recoup investments in R&D activities and productive infrastructure.

The greatest paradox is that the Cuban vaccine industry has remained absent from the global public sector markets serving the world's poorest populations, and instead has gone for the dollar, despite its focus on national public health, despite its medical diplomacy, despite its socialist ideology, and despite the fact that in theory such sales would be profitable. The most plausible explanation – an excessive cost level, one way or the other – forces us to conclude that even practical philanthropy sometimes may depend on the possession of a competitive edge. In this case the competitive edge would consist in the capability of producing vaccines in high volumes at very low cost.

One way of displaying the ambiguity of interests is presented in Table 4. The meningococcal vaccine was conceived of as a public health measure – the first quadrant – but subsequently it ended up in the fourth. The hepatitis B vaccine – apart from also being a strategic technology platform development project – was initially targeting the national market, but it is difficult to disentangle the commercial and public health considerations, since both would be served by that product. Later on also the hepatitis B vaccine generated substantial export revenues, but failed to enter the grey zone of being marketed at tiered prices at the global public sector markets. The more recent therapeutic cancer vaccines seem to be motivated primarily in the fourth quadrant, and since they are unique products and do not replace existing therapies like chemotherapy or radiation they have no place in the second, but to the extent that they become applied nationally they may also have a domestic public health impact (first quadrant). The meningococcal group A vaccine manufacturing assignment for the benefit of the countries in the Meningitis Belt in Africa also somehow falls in a grey zone between (or across) the third and fourth quadrant.

The full extent of the ambiguities is not even visible in the table, since the public health interests in the first quadrant sometimes may have to prioritize either modern or traditional health problems. Similarly, in order to further complicate the issue one could include diverging interests of different patient or social groups, which is beyond the scope here. We have also observed that strategic and techno-economic evaluations are performed in a continuous and reiterative process, and that the underlying interests are not necessarily stable over time.

Table 4. Ambiguous interests.

Application	Philanthropy		Commercialism
National	1 Public health		2 Import substitution
International	3 International aid	Tiered prices	4 Export revenue generation

The first sentence of this paper unilaterally associated the Cuban public health system to the values of philanthropy and humanitarianism, placing it squarely in the first quadrant, which appears as a contrast to the mixed interests that have been in play in the biotech sector. However, the Cuban health system is influenced by almost exactly the same interests as the biotech sector: the fact that close to 40,000 foreign medical students on scholarships have been trained in Cuba between 1961 and 2001 fits into the third quadrant. Huge numbers of Cuban doctors are working abroad on different assignments: some missions are part of Cuban humanitarian aid programs, sometimes funded by third parties (third quadrant); some missions are paid for by the host government (fourth quadrant); some missions are part of comprehensive packages involving trade and political agreements (third and fourth quadrant); and the dollar clinics in Havana (officially open to foreigners only) receive affluent patients from all over Latin America and the Caribbean (fourth quadrant). Since Cuba has never relied on imports of medical services, only the second quadrant is somehow irrelevant. In short, medical services exports generated approximately USD 1.5 billion worth of revenues in 2005 – slightly more than tourism (Feinsilver 2006), and almost six times more than the total biopharmaceutical exports.

The aim has not been to reconstruct concrete decision making processes, and apart from Fidel Castro himself the main powerful actors in terms of individuals remain anonymous and unseen. Although we do not know the exact details of the how-s, who-s, when-s, and where-s, some important why-s have been discussed, and it has been possible to infer some of the deliberations and considerations that have been made. Despite all the paradoxes and ambiguities, the 'triangulating' method of approaching interests of public health and commercialism from several different angles resulted in a relatively consistent narrative about some major strategic and techno-economic evaluations that have been performed in the Cuban biotech sector.

Michel Callon's model of techno-economic networks – with its concepts of strategic and techno-economic evaluations – turned out to be an appropriate tool for studying the political thinking underlying the Cuban biotech sector. In contrast to most other approaches in innovation studies, which focus on knowledge creation, interactive learning, and autonomous firms operating in a context of public and private institutions, the techno-economic network model deals explicitly with interests and strategic decisions – exactly the phenomena that were under study in this paper.

As already stated, one issue remains unresolved. The apparent switch of focus from modern to traditional disease patterns represented by the emergence of the Cuban vaccine industry may have been induced by the need to combat the acute and serious meningococcal epidemic that hit the island in the late 1970s. This hypothesis is elaborated on in detail in the other paper about the Cuban biotech sector (Plahte 2010).

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